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Fruits, Vegetables, and Cancer Prevention Trials

The negative results from intervention trials that sought to prevent cancer by use of β -carotene supplements underline the difficulty in choosing the appropriate prophylactic agent (1). Hind-sight, which is of course always 20-20, should have cautioned us that the association between β -carotene and cancer was just that, an association, and that association does not mean causation. But have the lessons from this saga really been learned?

It appears that many researchers are of the opinion that the β -carotene trials failed only because the wrong carotenoid was chosen or else was given at the wrong dose. I would argue that the problem is more fundamental. As discussed elsewhere (2), only weak evidence supports a major role for antioxidants in cancer. There are other equally plausible substances in fruits and vegetables that may be responsible, for instance, folate (3) and phytochemicals (4). Prostate cancer may be a special case where the protective substance is lycopene, a carotenoid found in tomatoes (5).

Clearly, if the research strategy is to conduct intervention trials, each using one substance at one dose, then it will probably take several decades to discover an effective anticancer substance. This is especially true if there is no "magic bullet" in fruits and vegetables but rather a "team" of substances, each of which is needed for optimal effectiveness.

Accordingly, the most appropriate step may be to conduct a randomized intervention trial using a mixture of fruits and vegetables. A suitable mixture might be oranges, tomatoes, broccoli, and carrots. A placebo of similar taste and appearance could easily be formulated. In addition to this rationale, such a trial would achieve the following objectives: 1) It would prove that fruits and vegetables do indeed prevent cancer, 2) it would demonstrate the feasibility of this study design, and 3) there is strong

evidence that fruits and vegetables should also prevent coronary heart disease (6) and help correct hypertension (7).

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REFERENCES

- (1) Greenwald P, McDonald SS. Antioxidants and the prevention of cancer. In: Basu TK. Temple NJ, Garg ML, editors. Antioxidants in human health and disease. Wallingford (UK): CAB International; 1999. p. 217–34.
- (2) Temple NJ. Antioxidants and disease: more questions than answers. Nutr Res. In press.
- (3) Giovannucci E, Stampfer MJ, Colditz GA, Hunter DJ, Fuchs C, Rosner BA, et al. Multivitamin use, folate, and colon cancer in women in the Nurses' Health Study. Ann Intern Med 1998;129:517–24.
- (4) Nestle M. Broccoli sprouts in cancer prevention. Nutr Rev 1998;56:127–30.
- (5) Giovannucci E, Clinton SK. Tomatoes, lycopene, and prostate cancer. Proc Soc Exp Biol Med 1998;218:129–39.
- (6) Law MR, Morris JK. By how much does fruit and vegetable consumption reduce the risk of ischaemic heart disease? Eur J Clin Nutr 1998: 52:549-56.
- (7) Appel LJ, Moore TJ, Obarzanek E, Vollmer WM, Svetkey LP, Sacks FM, et al. A clinical trial of the effects of dietary patterns on blood pressure. DASH Collaborative Research Group. N Engl J Med 1997;336:1117–24.

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More About: Sunscreen Use, Wearing Clothes, and Number of Nevi in 6- to 7-Year-Old European Children

The recent article by Autier et al. (1) and the accompanying editorial (2) have heightened interest in the relationship between sunscreen use and the incidence and prevalence of melanocytic lesions, including nevi and cutaneous melanoma.

In view of the concern about sunscreens and melanoma risk (3,4), we have analyzed data from the Western Canada Melanoma Study. This study is one of the largest and most detailed studies of melanoma, and it demonstrated clear associations with pigmen-

tation characteristics and tendency to sunburn (skin type), as well as with recreational and occupational sun exposure (5,6). It compared incident cases of melanoma diagnosed from 1979 through 1981 with population-based controls, using a home interview. Subjects were asked, "When exposed to sun on your skin, other than face and arms, do you use a suntan or anti-sunburn lotion or cream almost always, sometimes, only for the first few hours, or almost never?" Only three control subjects and no case patients responded "almost never." Before this analysis, we hypothesized that if sunscreens directly increase melanoma risk, risks will be highest in the "almost always" users, whereas if sunscreens are used to permit more intense sun exposure, risks will be highest in the "only for the first few hours" category. The risks were assessed as odds ratios for melanoma of the trunk or lower limb (369 case-control pairs), after adjustment for host factors and skin type, and for measures of sun exposure, using multiple logistic regression.

As shown in Table 1, compared with those using sunscreens "sometimes," which we interpret as the lowest degree of use, those reporting use "almost always" had an unchanged risk of melanoma, both in simple analysis and after adjustment for host factors (hair, eye, skin color, and skin type) and for measures of sun exposure. In contrast, those who reported use of sunscreens "only for the first few hours" had a statistically significantly increased risk of melanoma that was only slightly lowered and remained statistically significant, after adjustment for host factors and for sun exposure. Analyses of men and women separately showed very similar results, the adjusted odds ratios for sunscreen use only for the first few hours being 1.68 in men and 1.70 in women.

The results for the "almost always" users argue strongly against any direct increased risk of sunscreen use. The results for those who use sunscreens only for the first few hours suggest that such use provides inadequate protection against the increased risks due to sun exposure or host characteristics. This study was done before extensive publicity on the risks of sun exposure, which makes response bias less likely, although the types and usage patterns of sunscreen use may differ from current

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